

SUSCEPTIBILITY TO CANCER

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THE impressive statistics showing that cancer in the human species is increasing are at least open to question. Reliable computations show that a greater number of persons live to reach middle age or longer, when cancer is more common.

In countries that compile trustworthy statistics the incidence of cancer is approximately in the same ratio to population and sex, but there is considerable divergence in the different organs and tissues involved. In this country, about 30 per cent. of deaths from cancer among women is due to cancer of the breast and genitalia. In men the incidence in the genitalia is very low. On the basis of cancer of the generative organs, therefore, one would expect the total incidence of cancer in men to be considerably lower than in women, but the percentage is approximately the same, because in men the organs common to both sexes, such as the stomach and the organs of the urinary system, are more often affected by cancer than in women, and this increased frequency equalizes the high percentage of instances in which the breasts and uterus are the seat of cancer in women.

One of the few known facts about cancer is its relation to later life. In women the senile changes which take place in the breasts and uterus at the menopause are a factor in bringing about cell changes which invite cancer. The genitalia in men undergo no such sudden and profound senile changes; inasmuch as the testis is the primitive organ of procreation from which the ovary is derived, it has a protective heredity behind it.

It is worth while occasionally to go back and take account of stock, so to speak, to see what we really know about cancer that has stood the test of time.

We have thought of cancer so much in relation to the human being that we have not always kept clearly in mind that every living thing may suffer from an analogous disease. The late Dr. Erwin F. Smith, working in the government laboratories in Washington, found that cancer in plants had the essential characteristics of cancer in man, and he noted the relation of these types of plant tumors to certain bacteria which he believed to be the cause either of such cancers or of irritation in susceptible plants which resulted in those changes in cells which were responsible for the tumors.

The development of cancer in the lower animals has received a greater amount of study than cancer in plants, and is fairly well understood. The disease in the lower animals, again, exhibits the same general characteristics as in man: that is, cell changes, growth to the limit of obtaining blood supply, and transplantability in the same animal through metastatic processes, with which we are only too familiar.

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Cancer does not appear in sound tissues. Investigation of the various theories of the causation of cancer shows that the one provocative agent which remains unchallenged is chronic irritation. In all lands, among all peoples, we see this one causative influence in the ascendant. In China, among those who shave their heads with a dull and rough-edged razor, cancer of the scalp is common, but does not occur among those who do not shave the scalp. The Chinese men eat at the first table, when the rice is hot, throwing it with some force by means of chopsticks into the mouth and pharynx, and not infrequently they suffer from cancer of the pharynx and the beginning of the oesophagus. The women, who eat at the second table, when the rice is cold, seldom have the disease. In Australia the sharp-edged sand in the desert portion of the country, blown by the hot wind, so frequently produces cancers of the skin of the face that such cancers are called the "Australian disease." In certain parts of India and the Philippines, where the betel nut wrapped in its leaf with lime is chewed, cancer of the mucous membrane of the cheek is still common. Among smokers, cancer of the lip sometimes develops, less commonly since heat-conducting clay pipes are no longer used. Cancer of the gums and about the teeth is less common now that by modern methods of dentistry irritating stumps and roots may be removed. Cancer of the breast occurs largely among civilized women. In those countries in which the breasts are allowed to be exposed, that is, are not compressed or irritated by covering, it is rare. In the mountain regions of Kashmir, India, where the people carry braziers filled with hot coals strapped onto the lower part of the abdomen, cancer just above the pubis is common.

With improvements in construction of buildings and change in fuel, there are no longer many chimneys which require cleaning, so that chimney-sweep's cancer of the groin is less common, but we still see an occasional cutaneous epithelioma on the shins of railroad engineers and firemen whose legs have been exposed during years to the intense heat of the engine fire-box.

I have merely touched on these few outstanding examples of cancer of visible parts of the body about which there is little dispute. As to cancer of the interior of the body we have less definite proof, but cancerous gall-bladders usually contain stones, and that ulcer of the stomach may be responsible for cancer of the stomach is admitted by all, although there are great differences of opinion as to its frequency. Hurst has given statistics to show that in about 20 per cent. of cases of ulcer of the stomach, cancer may be expected. In our own experience, while the percentage in which the histologic examination of excised cancers of the stomach for evidence of preceding ulcer varies in different series of cases, the development of gastric cancer on some type of demonstrable precancerous disease such as ulcer is present in more than 25 per cent.

Cancer of the stomach in men constitutes a third of the total number of cancers in all parts of the body. The cause of the greater frequency of cancer of the stomach among men has not been solved. The men of the

rates that do not confine themselves to civilized customs are less often affected by cancer of the stomach. Do hot drinks change the gastric epithelium, or does food in large quantities wear out its secretory function so as to produce premature changes in the gastric epithelium? Cancer of the small intestine is rare as compared with cancer of the stomach, large intestine and rectum, which have a short heredity as compared with the primitive small intestine, and this may be a factor.

When we try to estimate the exact relationship of sources of chronic irritation to cancer, there are various explanations. Certain observers believe that the site of chronic irritation, unprotected by normal epithelium, permits the entrance of an outside agent, perhaps a microorganism, but if so, why should the metastatic process always show the histopathologic characteristics of the original lesion? A metastatic process in the liver from a cancer of the gastro-intestinal tract shows, not cancer of the liver, but a secondary cancer of the gastro-intestinal epithelium in the liver.

A possible explanation is that when the tissues have been subjected to a long-continued insult, the reparative processes are exhausted and, instead of healthy cells, less mature cells are thrown into the breach of continuity until finally embryonic cells are used to replace the normal epithelium.

New revelations would make it appear that cancer may be the result of agencies acting from within the body due to biochemical dysfunction affecting the life history of embryonic cells. In any event, it may be assumed that the agents which act on the cell to produce malignancy become an inseparable constituent of the cell, as metastasis takes place only by the transplantation of the malignant cell itself.

Individuals vary in their susceptibility to the cause or causes of cancer, whatever they may be. In no other way can we explain why 90 per cent. of persons do not have cancer, and why 10 per cent. of them die from it. It is as logical to accept the hypothesis that the 90 per cent. of persons have greater resistance to cancer than the 10 per cent., as to attempt to force an explanation of why only 10 per cent. come in contact with hypothetic causative agents. If the patient's susceptibility to the disease is the significant factor in the development of cancer, the site of the growth would be determined by the tissue or organ subjected to the insult of a precancerous lesion, and the grade of malignancy and the metastatic possibilities by the susceptibility of the body as a whole. Perhaps the reason cancer usually appears after middle life is that the cells of the body have lost the reparative power of youth, have a lessened immunity, and thereby have become more vulnerable.

Certain sources of chronic irritation seem to have greater potentiality to produce malignant disease than others, such as unrefined tar, which seems to possess more than ordinary powers of precancerous irritation for susceptible animals.

The local response of the tissue subjected to chronic irritation apparently is influenced by general systemic factors which may either accelerate or delay the development of cancer. Murray's work leads to the inference that there

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are variations in the resistance or, conversely, in the susceptibility of individual mice to cancer from tar painting. Slye found that by breeding strains of mice in which the disease developed most readily, the susceptibility of these strains could be increased enormously, so that mice would be born with the disease. By mating mice that were not so readily susceptible to cancer, strains could be developed in which cancer could not be produced and to which cancer could not be transferred.

The malignant cell has a remarkable resemblance to the rapidly growing embryonic cells of the chorionic villi (Langhans' cells). The stroma of a cancerous growth is the measure of nature's resistance. The greater the amount of stroma and the less the proportion of cells, the slower the growth. Wilson, MacCarty, and Broders have enlightened us greatly with regard to the histologic character of the cell in relation to malignancy. Wilson was able, twenty-five years ago, to develop an original polychrome methyl blue stain for frozen sections which gave good differential coloration of the various elements of the cell, thus making possible an immediate microscopic diagnosis. MacCarty called attention to the significant fact that the greater the proportion of the nucleus and the less the differentiation of the cell cytoplasm, the more rapid the growth of cells; that an excess of the nucleolar element is associated with the type of rapid growth and invasion which is clinically malignant. Broders, in a careful clinicopathologic study of the relative amounts of cell differentiation in a tumor, pointed out that the more nearly the cancer cell approaches normal, the less the malignancy, and was able to develop an index of malignancy. Bowing found from experience with radium and X-ray that the more severe grades of cancer, Grades 3 and 4 of Broders' classification, may sometimes be made to take on the more favorable aspects of the cancers of Grades 1 and 2, with definite slowing of the process, so that sometimes such a lesion primarily inoperable may become operable.

The assumption has always been that the more severe grades of cancer are due to a more potent cause. I hardly need point out that these newer revelations throw some doubt on so ready an explanation. It is equally, if not more, probable that the more severe forms of cancer and the development of cancer in certain tissues are due to increased susceptibility.

The foregoing studies logically lead to the idea of increasing individual resistance to the disease and its ultimate prevention. Science has been able to develop soil changers in smallpox, diphtheria and tetanus. Why not in cancer? Because of natural immunity to the disease relatively only a small proportion of the total population is susceptible to scarlet fever. With the Dick test the degree of natural immunity of the individual to scarlet fever can be determined, and if it is not sufficient to protect from the disease, it can be increased to normal by serum. Why not in cancer? Perhaps the development of cancer as well as its degree of malignancy is attributable to the diminished activity of immunizing processes rather than to the nature of the activating agent.